PBTC-004 Abstract for Health Professionals

Study Title: Phase I Study of Intrathecal Spartaject™-Busulfan in Children with Neoplastic Meningitis

Description:

The alkylating agent busulfan is an extremely hydrophobic compound that precludes intravenous (IV) or intrathecal (IT) administration. Spartajectä -Busulfan is a phospholipid-encapsulated form of busulfan that can be easily dispersed in water and hence makes it amenable to IT or IV therapy. This phase I study of IT Spartajectä -Busulfan is designed to evaluate the toxicity and pharmacokinetics of administering this drug intrathecally in children with refractory leptomeningeal disease from primary malignant brain tumors, acute lymphoblastic leukemia, and lymphoma.

Objectives:

1. To determine the qualitative and quantitative toxicity of intrathecal Spartaject™-Busulfan when administered to children and adolescents with a refractory CNS malignancy.
2. To determine the maximum-tolerated dose (MTD) of intrathecal Spartaject™ -Busulfan that can be recommended for subsequent phase II studies.
3. To determine the cerebrospinal fluid (CSF) and serum pharmacokinetics of Spartaject™-Busulfan following IT administration.

Rationale:

The following factors favor the use of intrathecal busulfan in children with leptomeningeal disease from primary malignant brain tumors:

- The activity of busulfan in brain tumor xenografts in athymic mice at clinically achievable plasma concentrations
- The lack of cross-resistance between busulfan and other alkylating agents including cyclophosphamide and nitrosoureas.
- Responses observed with IT busulfan in adult patients with meningeal carcinomatosis

Eligibility Criteria:

- Histologically confirmed diagnosis of a neoplasm that is metastatic in the CSF or leptomeningeal subarachnoid space

- Age >= 2 years and <= 21 years of age

- Evidence of tumor: There must be a cytological diagnosis of malignancy in the CSF and/or MRI evidence of leptomeningeal tumor in the brain or spine

- Prior therapy: No myelosuppressive chemotherapy within 3 weeks and no intrathecal chemotherapy in the one-week (2 weeks for prior DTC-101 therapy) prior to study entry. No focal irradiation to the CNS within one week and craniospinal irradiation within 8 weeks of study entry.

- Hematology: Absolute Neutrophil Count (ANC) >= 1000/mm^3 and platelets > 75,000/mm^3 prior to study entry; patients with bone marrow disease will not be eligible for this study

- Blood chemistries: SGOT/PT less than 5 times upper limit of institutional normal values; bilirubin within normal range, normal renal function with serum creatinine <= 1.5 times normal value.

- CSF flow: Patients with brain tumors require a normal CSF flow study. Patients with obstruction to or compartmentalization of CSF flow on a CSF flow study are not eligible for this study.

Contact:

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